Claims

1. A method for identifying therapeutic compounds, said method comprising:

(i) providing test cells that express a target protein containing a DEF domain and a MAP kinase,

(ii) culturing said cells in the presence of a growth factor, cytokine, tumor promoter, or oncogene,

(iii) contacting said cells with a candidate compound, and

(iv) assessing the binding of said MAP kinase to said DEF domain relative to the binding in the absence of said candidate compound, wherein a candidate compound that inhibits said binding is identified as a therapeutic compound.

2. The method of claim 1, wherein said DEF domain comprises the amino acid sequence F-X-F-P (SEQ ID NO: 1).

3. The method of claim 1, wherein said test cells are selected from the group consisting of fibroblasts, a primary cell line, an immortalized cell line, and a tumor-derived cell line.

4. The method of claim 1, wherein said growth factor, cytokine, tumor promoter, or oncogene is selected from the group consisting of epidermal growth factor (EGF), transforming growth factor α, heparin-binding-like EGF, heregulin, amphiregulin, epiregulin, cripto, PDGF-AA, PDGF-BB or PDGF-CC, insulin, insulin-like growth factors, fibroblast growth factors, colony stimulating factor, heaptocyte growth factor, a chemokine, an interleukin, lysophosphatidic acid, a phorbol ester, okadaic acid, microcystin, vanadate, hydrogen peroxide, calyculin A, Erb2/neu, sis, kit, Ras, Raf, PI3-kinase, and PTEN.

5. The method of claim 1, wherein said MAP kinase is extracellular signal-regulated kinase 1/2 (ERK1/2).

6. The method of claim 1, wherein said binding is assessed by detecting a DEF domain-dependent phosphorylation.

7. The method of claim 1, wherein said target protein is a Fos, Myc, or Jun family protein.

8. The method of claim 7, wherein said target protein is c-Fos.

9. The method of claim 8, wherein said step (vi) comprises assessing the phosphorylation of T325 or T331.

10. The method of claim 8, wherein said step (vi) comprises an antibody that specifically binds to phospho-T-325 c-Fos.

11. The method of claim 1, wherein said therapeutic is useful for the treatment of cancer and said target protein comprises the sequence of a protein identified in Tables 1 or 2.

12. The method of claim 1, wherein said therapeutic is useful for the treatment of a cardiovascular disorder and said target protein comprises the sequence of a protein identified in Table 3.

13. The method of claim 1, wherein said therapeutic is useful for the treatment of an inflammatory disorder, and said target protein comprises the sequence of a protein identified in Table 4.

14. The method of claim 1, wherein said therapeutic is useful for the treatment of a metabolic disorder, and said target protein comprises the sequence of a protein identified in Table 5.

15. The method of claim 1, wherein said therapeutic is useful for the treatment of a neuropathy or a behavioral disorder, and said target protein comprises the sequence of a protein identified in Table 6.

16. The method of claim 1, wherein said therapeutic is useful for the treatment of a sleep disorder, and said target protein comprises the sequence of a protein identified in Table 7.

17. A method for identifying a therapeutic compound, said method comprising:

(i) providing a sample comprising a target protein comprising a DEF domain, a MAP kinase, and a candidate compound,

(ii) contacting said target protein, said MAP kinase, and said candidate compound,

(iii) assessing the binding of said MAP kinase to said DEF domain in said sample in the presence of said candidate compound relative to binding in the absence of said candidate compound, wherein a compound that inhibits binding of said MAP kinase to said target protein is identified as a therapeutic compound.

18. The method of claim 17, wherein said DEF domain comprises the amino acid sequence F-X-F-P (SEQ ID NO: 1).

19. The method of claim 17, wherein said MAP kinase is extracellular signal-regulated kinase 1/2 (ERK1/2).

20. The method of claim 17, wherein said binding is assessed by detecting a DEF domain-dependent phosphorylation.

21. The method of claim 17, wherein said target protein is a Fos, Myc, or Jun family protein.

22. The method of claim 21, wherein said target protein is c-Fos.

23. The method of claim 22, wherein said target protein is c-Fos and step (vi) comprises assessing the phosphorylation of T325 or T331.

24. The method of claim 22, wherein said step (vi) comprises an antibody that specifically binds to phospho-T-325 c-Fos.

25. The method of claim 17, wherein said therapeutic is useful for the treatment of cancer and said target protein comprises the sequence of a protein identified in Tables 1 or 2.

26. The method of claim 17, wherein said therapeutic is useful for the treatment of a cardiovascular disorder and said target protein comprises the sequence of a protein identified in Table 3.

27. The method of claim 17, wherein said therapeutic is useful for the treatment of an inflammatory disorder, and said target protein comprises the sequence of a protein identified in Table 4.

28. The method of claim 17, wherein said therapeutic is useful for the treatment of a metabolic disorder, and said target protein comprises the sequence of a protein identified in Table 5.

29. The method of claim 17, wherein said therapeutic is useful for the treatment of a neuropathy or a behavioral disorder, and said target protein comprises the sequence of a protein identified in Table 6.

30. The method of claim 17, wherein said therapeutic is useful for the treatment of a sleep disorder, and said target protein comprises the sequence of a protein identified in Table 7.

31. The method of claim 17, wherein said target protein further comprises a fluorescent moiety.

32. A method for treating a cancer in a mammal, said method comprising administering a therapeutically effective amount of a compound that inhibits the binding of a MAP kinase to the DEF domain of a target protein.

33. The method of claim 32, wherein said MAP kinase is ERK1/2.

34. The method of claim 32, wherein said target protein is an immediate early gene.

35. The method of claim 32, wherein said target protein is selected from the group consisting of c-Fos, Fra-1, Fra-2, c-Myc, N-Myc, JunD, JunB, and c-Jun.

36. The method of claim 35, wherein said target protein is c-Fos.

37. The method of claim 32, wherein said target protein is a protein identified in Tables 1 or 2.

38. The method of claim 32, wherein said cancer is selected from the group consisting of leukemia, Hodgkin's disease lymphoma, non-Hodgkin's disease lymphoma, fibrosarcoma, liposarcoma, osteogenic sarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, Wilm's tumor, cervical cancer, uterine cancer, testicular cancer, small cell lung carcinoma, non-small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, schwannoma, meningioma, melanoma, neuroblastoma, and retinoblastoma.

39. A method for treating cardiovascular disease in a mammal, said method comprising administering a therapeutically effective amount of a compound that inhibits the binding of a MAP kinase to the DEF domain of a target protein.

40. The method of claim 39, wherein said MAP kinase is ERK1/2.

41. The method of claim 39, wherein said target protein is a protein identified in Table 3.

42. The method of claim 39, wherein said cardiovascular disease is selected from the group consisting of ischemic heart disease, ventricular heart failure, cardiac hypertrophy, hypertension, and atherosclerosis.

43. A method for treating an inflammatory disorder in a mammal, said method comprising administering a therapeutically effective amount of a compound that inhibits the binding of a MAP kinase to the DEF domain of a target protein.

44. The method of claim 43, wherein said MAP kinase is ERK1/2.

45. The method of claim 43, wherein said target protein is a protein identified in Table 4.

46. The method of claim 43, wherein said inflammatory disorder is selected from the group consisting of anaphylaxis, septic shock, allergic rhinitis, asthma, atopic dermatitis, and food allergies. Examples of autoimmune disorders include, but are not limited to, type 1 insulin-dependent diabetes mellitus, inflammatory bowel disease, Crohn's disease, ulcerative colitis, dermatitis, meningitis, thrombotic thrombocy topenic purpura, Sjögren's syndrome, encephalitis, uveitis, leukocyte adhesion deficiency, rheumatoid and other forms of immune arthritis, rheumatic fever, Reiter's syndrome, psoriatic arthritis, progressive systemic sclerosis, primary biliary cirrhosis, pemphigus, pemphigoid, necrotizing vasculitis, myasthenia gravis, multiple sclerosis, lupus erythematosus, polymyositis, sarcoidosis, granulomatosis, vasculitis, pernicious anemia, CNS inflammatory disorder, antigen-antibody complex mediated diseases, autoimmune hemolytic anemia, Hashimoto's thyroiditis, Graves disease, habitual spontaneous abortions, Reynard's syndrome, glomerulonephritis, dermatomyositis, chronic active hepatitis,

celiac disease, autoimmune complications of AIDS, atrophic gastritis, ankylosing spondylitis and Addison's disease.

47. A method for treating a metabolic disorder in a mammal, said method comprising administering a therapeutically effective amount of a compound that inhibits the binding of a MAP kinase to the DEF domain of a target protein.

48. The method of claim 47, wherein said MAP kinase is ERK1/2.

49. The method of claim 47, wherein said target protein is a protein identified in Table 5.

50. The method of claim 47, wherein said metabolic disorder is selected from the group consisting of diabetes, obesity, jaundice, polycystic kidney and hepatic disease, pancreatitis, Graves' disease, and Werner's syndrome.

51. A method for treating a neuropathy or behavioral disorder in a mammal, said method comprising administering a therapeutically effective amount of a compound that inhibits the binding of a MAP kinase to the DEF domain of a target protein.

52. The method of claim 51, wherein said MAP kinase is ERK1/2.

53. The method of claim 51, wherein said target protein is a protein identified in Table 6.

54. The method of claim 51, wherein said neuropathy or behavioral disorder is selected from the group consisting of diabetic neuropathy, muscular dystrophy, Williams Beuren's Syndrome, psychosis, schizophrenia, autism, Down's Syndrome, Parkinson's Disease, Alzheimer's Disease, epilepsy, Cockayne syndrome, bipolar disorders, depression, and opiate addiction.

55. A method for treating a sleep disorder in a mammal, said method comprising administering a therapeutically effective amount of a compound that inhibits the binding of a MAP kinase to the DEF domain of a target protein.

56. The method of claim 55, wherein said MAP kinase is ERK1/2.

57. The method of claim 55, wherein said target protein is a protein identified in Table 7.

58. The method of claim 55, wherein said sleep disorder is selected from the group consisting of advanced sleep phase disorder, delayed sleep phase disorder, insomnia, and narcolepsy.

59. An antibody that specifically binds to phospho-T-325 c-Fos.

60. The antibody of claim 59, wherein said antibody is polyclonal.

61. The antibody of claim 59, wherein said antibody is monoclonal.